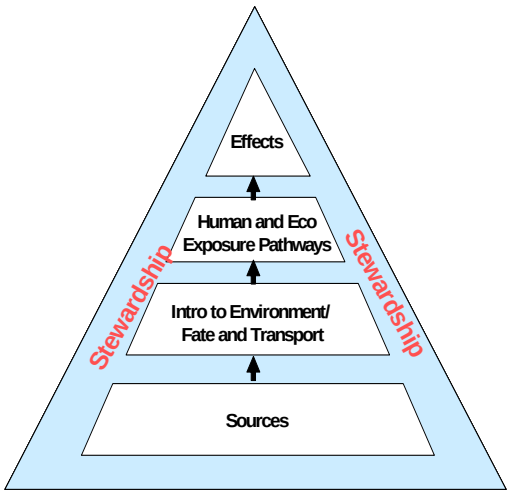
Attachment
EPA Office of Research and Development:
Research Efforts Related to Pharmaceuticals in the Environment

The research related to pharmaceuticals in the environment that is conducted by U.S. EPA's Office of Research and Development (ORD) is organized around the Research Framework under development by the Office of Science and Technology Policy Interagency Working Group on Pharmaceuticals in the Environment (see Figure). EPA has multiple research programs (e.g., Endocrine Disruptors, Drinking Water, Water Quality, Human Health), under which a number of efforts are related to or can be applied to pharmaceuticals in the environment and are helping inform the scientific issues.



In 2008, ORD is projected to commit $2.9 million on research related to pharmaceuticals. Much of the work is carried out by EPA scientists at several of the ORD national laboratories. ORD is also supporting new science on pharmaceuticals and other endocrine disruptors by engaging the broader research community through extramural grant programs. The Science to Achieve Results (STAR) grants program funds targeted research grants and graduate fellowships in numerous environmental science and engineering disciplines through a competitive solicitation process and independent peer review. The Small Business Innovation Research (SBIR) program has funded projects focused on identifying new approaches for detecting contaminants and assessing their endocrine disrupting ability.

The EPA research either completed or currently underway is intended to inform the Agency about the following elements of the framework:

Sources There are many potential sources for pharmaceuticals to enter into the environment. Some potential sources include wastewater treatment plant discharges, concentrated animal feeding operations (CAFOs), land applications (e.g., biosolids) and direct disposal/introduction to environment. Example:

- EPA researchers are collaborating with scientists funded through the Agency's STAR grant program, and from the US Geological Survey to characterize: 1) the extent to which CAFOs are sources of hormones (natural and pharmaceutical) in the environment, 2) their fate and transport and 3) the impact they have on aquatic organisms; and to develop approaches to mitigate exposures, where warranted.

Fate and transport When a pharmaceutical is introduced into the environment, it may undergo chemical reactions to form a new substance (fate) and be physically transported to another location in the environment (transport) with the potential for distribution/deposition into other media. Important considerations include the temporal pattern of introduction (e.g., periodic, persistent) and the potential for bioaccumulation in environmental media (e.g., sediments) or aquatic organisms. Example:

- Through its STAR program, EPA provided awards to six academic institutions to study the occurrence, fate and transport of a variety of pharmaceuticals and personal care products.

Exposure Pathways: Human and Ecological When an individual human comes in contact with a foreign chemical or substance, he or she becomes exposed, whereby the chemical may be transferred from the environment onto/into the individual. The major route of human exposure considered in the draft Framework is ingestion (drinking water or fish), although others may also be considered (e.g., dermal). For aquatic organisms, the main routes of exposure to be considered are dermal and ingestion. Example:

- EPA researchers participated in a study with a team of Canadian scientists who treated an experimental lake with ethynylestradiol (a pharmaceutical commonly found in birth control pills) to produce a chronic exposure to aquatic organisms at a level consistent with that observed in some wastewater treatment effluents. EPA used this opportunity to further develop a molecular assay as an indicator of estrogen exposure and to investigate the effects of long-term exposure to an endocrine-disrupting pharmaceutical in a whole lake ecosystem.

Ecological Assessment The process of determining whether a given chemical (e.g., a pharmaceutical) has an impact on biota or the ecosystem is known as ecotoxicology. This process, when completed for the broader ecosystem scale is an ecological assessment. Example:

- EPA has been conducting research concerning the ecological effects of a subset of human and veterinary reproductive and developmentally toxic pharmaceuticals using multiple small fish and amphibian species. Specific pharmaceuticals tested include the estrogens ethynylestradiol and estradiol (used in humans and, in the latter case, animals as well), the androgenic steroid trenbolone (used for livestock), the anti-androgenic compound flutamide (used for treating prostate cancer) and several drugs that affect natural steroid production such as fadrozole (developed to treat breast cancer), trilostane and ketoconazole. In addition, EPA has been involved in assessing the effects of endocrine-active pharmaceuticals in the field investigating, for example, the occurrence and potential population-level effects (on fish) of trenbolone emanating from CAFOs and estrogenic compounds associated with wastewater treatment effluents.

Human Health Assessment Human health assessment refers to the process of identifying potential health effects associated with a given exposure and then determining the dose-response relationship to characterize the associated risk. Example:

- EPA has ongoing research across multiple programs that are developing the methods, models, and measures that could be applied to the pharmaceuticals issue to assess potential impacts on human health. Some of these activities include: developing multiple short term and longer term assays (*in vitro* and *in vivo* in laboratory animal models) to identify potential endocrine disruptors, studying the effects of long term exposures to low levels of chemicals, and developing methods for cumulative assessments for chemicals that act through similar and different modes of action.

Managing Contaminants If human exposure to contaminants is found to pose a risk, it will be important to identify management approaches for minimizing their occurrence in water. Example:

- In order to establish a baseline understanding, EPA research is determining the effect of different drinking water treatment technologies currently in use on compound removal by examining the occurrence and fate of pharmaceuticals and other wastewater derived compounds through drinking water treatment.

A more complete list of ORD research projects, which includes a description of each project, is available on EPA's web site at www.epa.gov/ppcp/projects.